



Applicant: Harry V. Gelboin et al.

Title: Agents That Bind To And Inhibit Human Cytochrome ...

Attorney Docket No. 015280-389200US

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	P450						
	2C8	2C9*1	2C9*2	2C9*3	2C18	2C19	*others
MAB/P450							
MAb 292-2-3	-	-	-	-	-	-	-
MAB 592-2-5	-	++	+++	++	+++	-	-
MAB 5-7-5	+	++	+++	++	+	++	-
MAB 5-1-5	++	-	-	-	-	-	-
MAB 281-1-1	++	-	-	-	-	-	-
MAB 763-15-20	++	++	+++	++	-	-	-

\*other P450's include 1A1, 1A2, 2A6, 2B6, 2D6, 2E1, 3A4, 3A5  
(-) signifies no activity

**FIG. 1**

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	P450					
	2C8	2C9*2	2C9*1	2C18	2C19	*other P450s
MAb/P450						
MAb 292-2-3	0	92.5	11.0	0	0	0
MAb 592-2-5	0	90.8	80.6	82.0	0	0
MAb 5-7-5	0	96.0	91.3	93	95	0
MAb 5-1-5	96.0	0	0	0	0	0
MAb 281-1-1	91.0	0	0	0	0	0
MAb 763-15-5	0	90	88.2	30	0	0

FIG. 2

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MAb	P450			
	2C8	2C9 <sub>Cys144</sub> (*2)	2C18	2C19
MAb 292-2-3	0	91	0	0
MAb 592-2-5	0	88	66	0
MAb 5-7-5	0	93	93	93
MAb 5-1-5	91.6	0	0	0
MAb 281-1-1	91.8	0	0	0

FIG. 3

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MAB	Immuno Binding	h2C8	h2C9*1	h2C9*2	h2C9*3	h2C18	h2C19	Inhibits
MAB 292-2-3	ELISA	-	-	+++	-	-	-	2C9*2
	IB	-	-	-	-	-	-	
MAB 592-2-5	ELISA	-	++	+++	++	+	-	2C9/18
	IB	-	++	+++	++	+++	-	
MAB 5-7-5	ELISA	-	++	+++	++	+++	+++	2C9/18/19
	IB	+	++	+++	++	+	++	
MAB 5-1-5	ELISA	++	-	-	-	-	-	2C8
	IB	++	-	-	-	-	-	
MAB 281-1-1	ELISA	++	-	-	-	-	-	2C8
	IB	++	-	-	-	-	-	

FIG. 4

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2C9 Alleles  
2C9\*1-Arg144  
2C9\*2-Cys144  
2C9\*3-Leu359

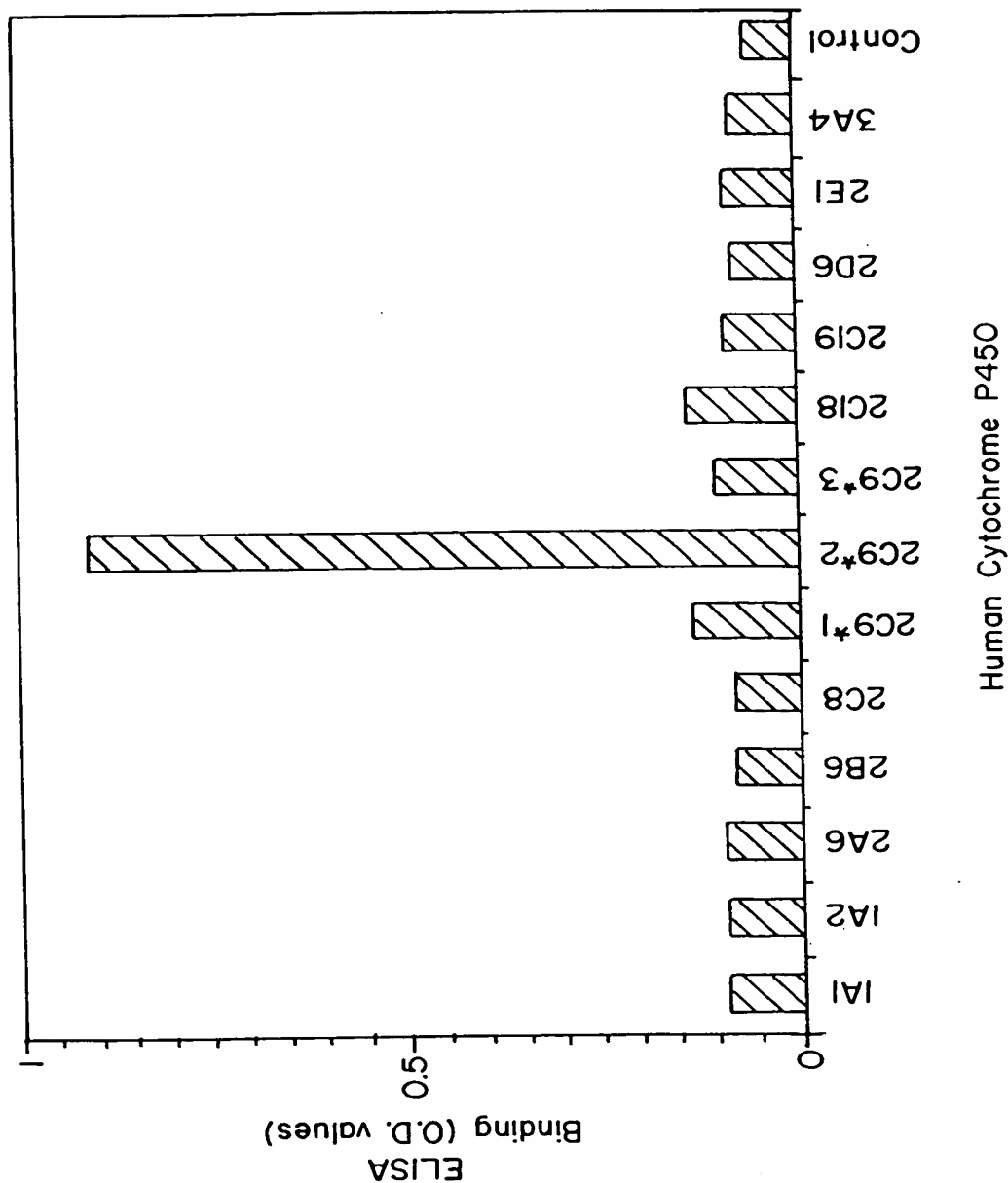


FIG. 5

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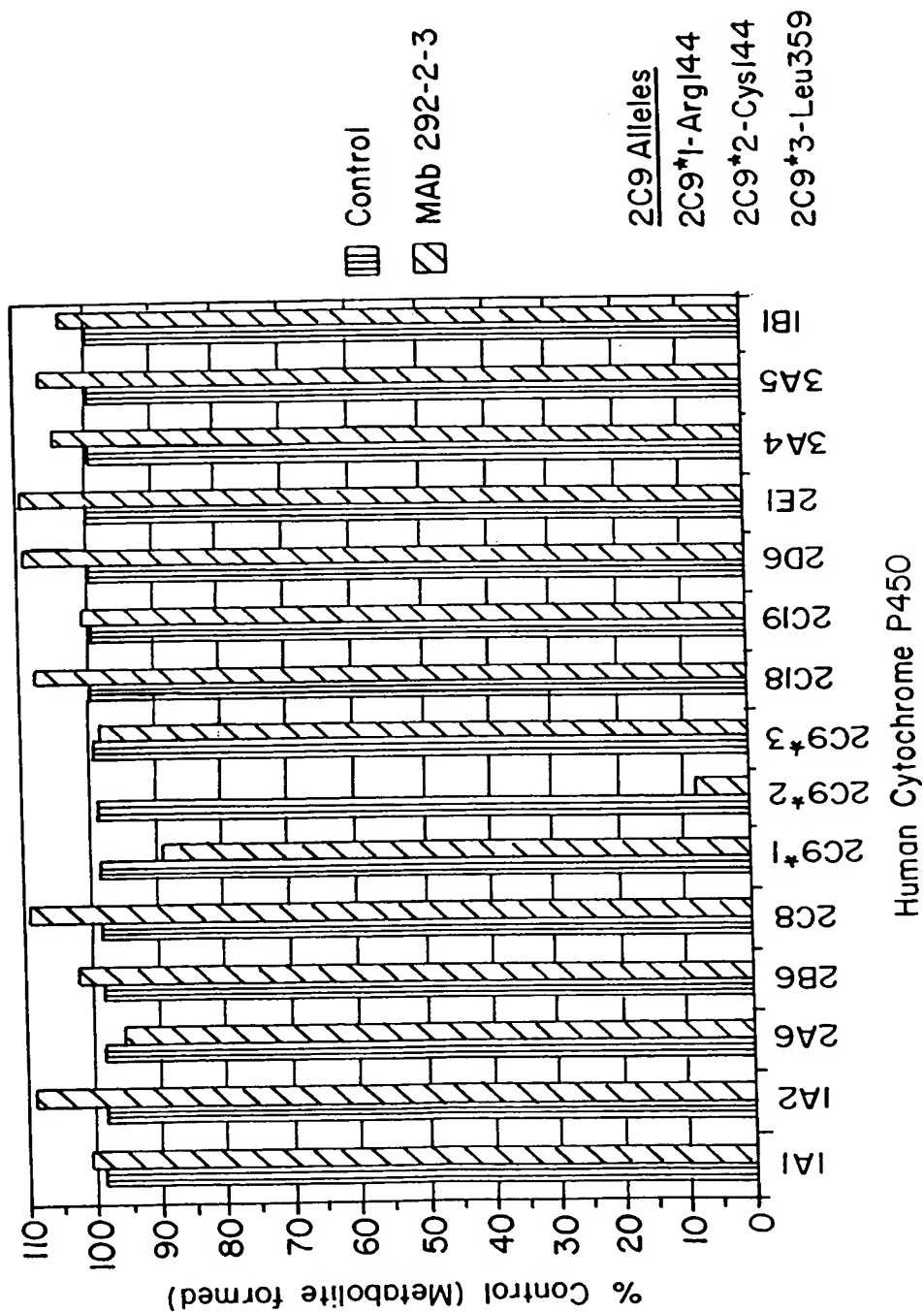


FIG. 6

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2C9 ALLELE<sup>^</sup>

	*1 - WT Arg144			*2 - Arg144Cys			*3 - Ile359Leu		
	Control	+ MAb	% Inh	Control	+ MAb	% Inh	Control	+ MAb	% Inh
<u>Substrate</u>									
Tolbutamide	1.0	0.98	1.3	0.85	0.03	96.4	0.22	0.02	9.3
Diclofenac	0.3	0.3	0.1	0.42	0.02	95.1	0.35	0.30	14.4

<sup>^</sup>P450 activity is(nmolproduct/min/nmolP450)**FIG. 7**

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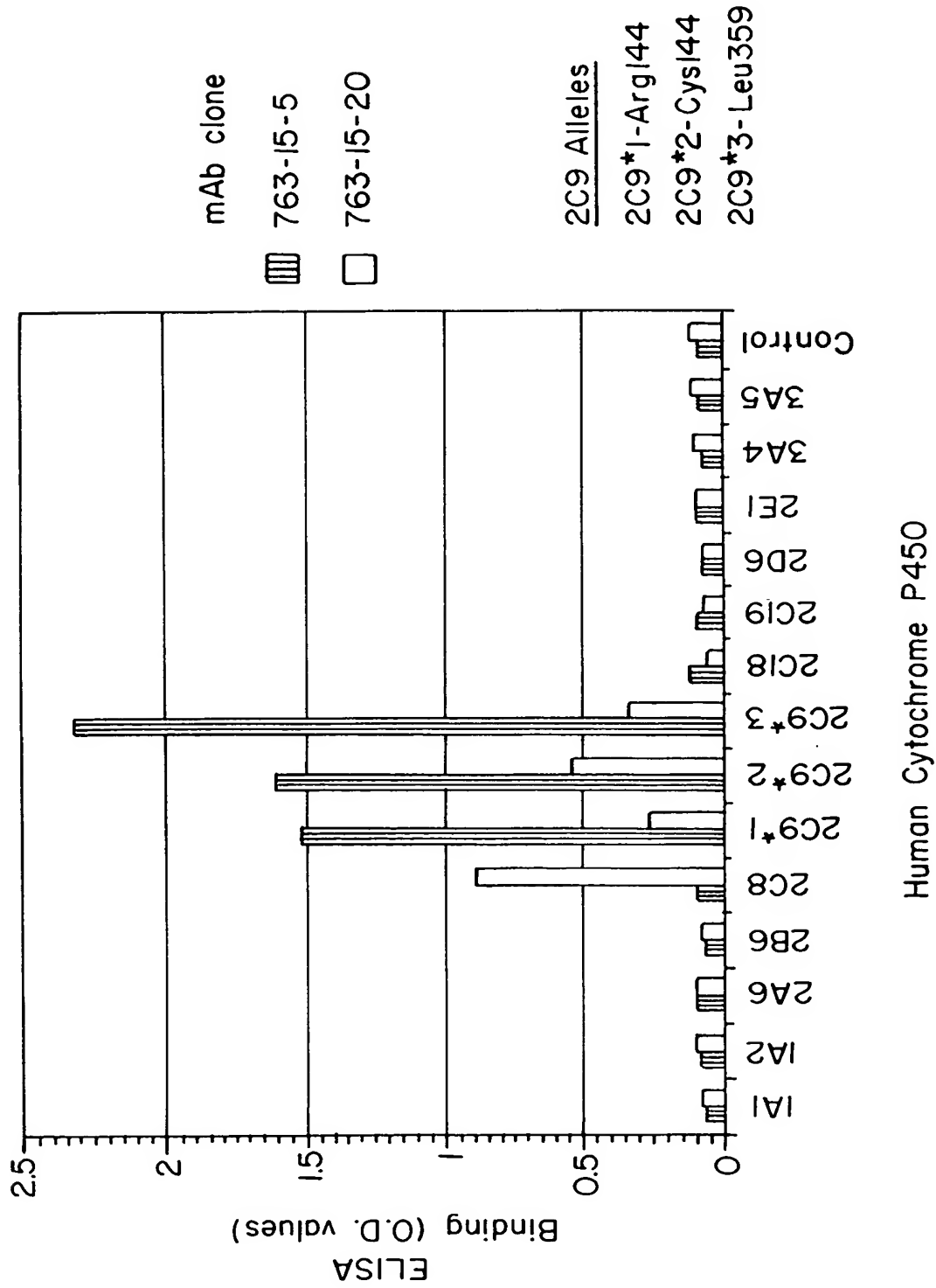


FIG. 8



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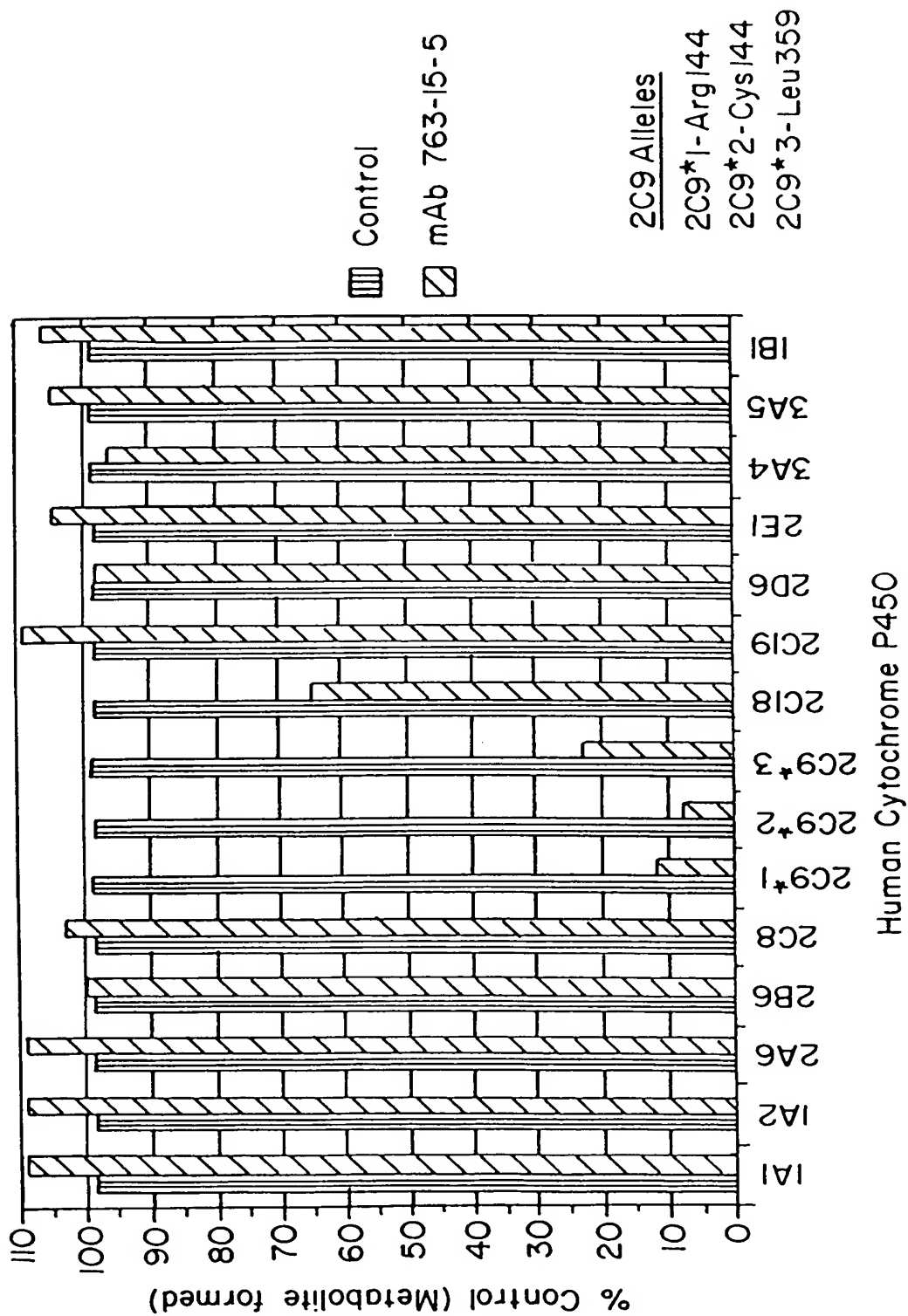


FIG. 9

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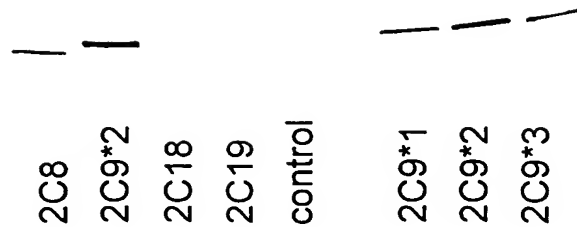
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No Blot

MAb 763-15-5



2C9 Alleles

2C9\*1-Arg144

2C9\*2-Cys144

2C9\*3-Leu359

MAb 763-15-20

**FIG. 10**

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% Inhibition of enzyme

Mab clone	2C9 <sub>Arg144</sub>	2C9 <sub>Cys144</sub>	2C9 <sub>Arg144</sub> Leu359
763-15-5	77.4%	93.2%	77.3%
763-15-20	5.5%	11.2%	0.2%

**FIG. 11**